

Remarks:

Claims 1 to 15 and 17 to 30 are pending.

Claim 16 has been canceled, as requested by the Examiner.

Rejection under 35 USC 101

The Examiner rejected claims 1-15, 17-19, 22-26, and 28-30 under 35 USC 101 as being drawn to non-statutory subject matter. In particular, the Examiner asserts that these claims lack a tangible result.

Claim 1 has been amended, among others, to recite “storing, at at least one computing device, a candidate statistical model ...”, where the underlined “at” was omitted due to a clerical error in the previous response filed April 1, 2007. Thus, it is clear now that the candidate model, necessarily including its optimized parameters, is stored at the at least one computing device. This is a “tangible” result: a computing system storing a statistical model for predicting disease risk. The stored candidate model permits its functionality to be realized in a practical application to produce a real-world result – to predict a disease risk to a particular member of the population, as recited in Claim 1. The Guidelines in MPEP 2106 do not require that a tangible result be “communicated to a user” or “output”. Rather, in MPEP 2106, subsection IV(C)(2)(2)(b) “Tangible Result”, it is stated that

The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. However, the tangible requirement does require that the claim must recite more than a 35 U.S.C.101 judicial exception, in that the process claim must set forth a practical application of that judicial exception to produce a real-world result.

Further, storing the statistical model “at” at least one computing device necessarily changes the state of the at least one computing device, and thus constitutes a “transformation” of a physical object to a different state (See MPEP 2106, subsection IV(C)(2)(A). Therefore, it is respectfully submitted that amended claim 1, and its dependent claims, are directed to statutory subject matter.

Amended claim 28 similarly recites “storing, at at least one computer, a plurality of statistical models...”, one of which is selected as a risk prediction model for predicting disease risk. Thus, it is submitted that amended claim 28, and its dependent claims, also produce a tangible result and are drawn to statutory subject matter.

New Matter

The Examiner rejected claims 1-15 and 17 to 30 under 35 USC 112, first paragraph, as introducing new matter. The underlined features identified by the Examiner are supported, as noted in the previous response filed April 1, 2007, at least in Figs. 1 and 7, and at paragraphs [0039], [0088], [0089], and [0090] of the description, which include the following description:

[...] an optimal candidate model **116** may be determined for a given combination of genetic data, by fitting non-genetic data **112** in all data sets **104** to the candidate model and optimizing the parameters [...] Each data set **104** is given a statistical significance corresponding to its corresponding weight **114**.[]

[...] candidate models **708** may be functions of non-genetic indicators **112** that can be used to predict the disease status (DS) of subjects **106** in the reference group **508**. That is, given the values of non-genetic indicators of a subject **106** in the reference group **508**, each of the candidate function can be used to calculate a value of DS **710** for the subject **106**. A fitting criterion may be the sum of weighted deviates **712**

$(\sum_{i=1}^n \Delta_i)$ of the fits. A deviate is the difference between an observed value and the corresponding predicated value. In the example illustrated, the observed values are the values of disease status indicator **109** in the collected data sets **104** and the predicted values are the values of indicator **710** calculated using the candidate models **708**. A weighted deviate (Δ_i) is a function of the deviate and the corresponding weight **114** of the relevant data set **104**. For example, the weighted deviate may be a product of the deviate and the corresponding weight **114**, i.e., $\Delta_i = w_i |DS_{\text{predicted}} - DS_{\text{observed}}| = w_i |r_i|$. [...] As can be appreciated, the corresponding weight **114** of a data set **104** determines the statistical significance of the data set **104**

[emphasis added].

Specifically, the Examiner alleges that there is no support for “calculating for each of said sets, a deviate of a predicted risk from an indicator of disease status for that set, said predicted risk predicted using said candidate model and non-genetic data”. In the exemplary embodiment described in the above quoted paragraphs, for each data set (as indicated by index “i”), a weighted deviate (Δ_i) is calculated from “ $\Delta_i = w_i |DS_{\text{predicted}} - DS_{\text{observed}}|$ ”. The predicted risk for each data set (value of DS **710** or $DS_{\text{predicted}}$) is calculated using a candidate model **708**, which may be “functions of non-genetic indicators **112**”. The indicator of disease status for each data set is DS_{observed} . This embodiment thus clearly supports the above cited limitation.

The Examiner also alleges that there is no support for “calculating a sum of weighted deviates for all of said sets, wherein each deviate is weighted in said sum by the weight associated with that set for which said each deviate has been calculated”. The above-quoted paragraphs disclose the calculation of “the sum of weighted deviates **712** $(\sum_{i=1}^n \Delta_i)$ ” for all data sets (as indicated by $i = 1$ to n), that a “weighted deviate (Δ_i) is a

function of the deviate and the corresponding weight **114** of the relevant data set **104**", and that the "weighted deviate (Δ_i) may be a product of the deviate and the corresponding weight **114**, i.e., $\Delta_i = w_i |DS_{\text{predicted}} - DS_{\text{observed}}| = w_i |r_i|$ "; .thus providing support for the cited limitation.

Further support for these limitations can also be found in claims 4 to 8 as filed.

Therefore, withdrawal of the new matter rejection is respectfully requested.

Rejection under 35 USC 112, 2nd paragraph

Claims 1, 27 and 28 have been amended to insert "at" before "at least one" in the various expressions identified by the Examiner, thus addressing the rejections thereto.

Claim 3 has been amended to clarify that the weighted deviate is obtained by multiplying the corresponding weight and a function of the corresponding deviate, thus addressing the Examiner's rejection.

The Examiner rejected Claim 13 on the basis that "it is unclear to what 'extent' the adjustment factors indicate the weights representative of members". Claim 13 has been amended to delete the objected to wording. Thus, withdrawal of this rejection is respectfully requested.

Rejection under 35 USC 103

Claims 1, 2, 3, 9, 19, 20, 21, 23 and 28 to 30 are rejected under 35 USC 103(a) as obvious having regard to Dodds *et al.* ("Dodds") in view of Luciano *et al.* ("Luciano").

In MPEP 2143, it is provided that to establish a *prima facie* case of obviousness, three basic criteria must be met:

- (1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.
- (2) There must be a reasonable expectation of success.
- (3) The prior art reference (or references when combined) must teach or suggest all the claim limitations.

The Examiner admits that Dodds does not disclose “optimizing model parameters by minimizing the sum of weighted deviates, where the deviates are weighted by corresponding weights that reflect genetic data associated with the respective data sets” (emphasis added). The Examiner has not pointed to any specific text in Luciano that discloses this feature, particularly the underlined portion. In fact, the Examiner has not expressly asserted that Luciano discloses this feature but only states that Luciano discloses a method which includes optimization of model parameters, and discloses calculations based on summation of weighted deviations that incorporate estimated and actual data. Careful review of the Luciano reveals that Luciano does not disclose or suggest this feature (see below). Thus, it is respectfully submitted that the Examiner has failed to establish a *prima facie* case of obviousness, because the cited references do not disclose or suggest all the claimed limitations.

Further, the Examiner is of the view that it would have been obvious to practice the method of Dodds with the additional model optimization steps taught by Luciano and asserts that such a combination results in “the practice of the instant claimed invention.” Applicants respectfully disagree with this assertion for at least the following reasons.

As recited in, e.g., claim 1, the disease risk is calculated from the model “as a function of non-genetic data”, and “the weights associated with data sets having like genetic

data are the same". Conveniently, the claimed invention provides an advantage in that the impacts/effects of both genetic data and non-genetic data are taking into account, but separately. As discussed at paragraph [0095] of the present application, "by using this method it is possible to analyze genetic data and non-genetic data separately, without having to directly untangle the interwoven and intractable relationship between them, and yet not ignoring the effects of either. Also, it is possible to significantly reduce the amount of computation in the case of a large number of risk factors, as only data indicative of a subset of the risk factors is analyzed at a time." See also the discussion at paragraphs [0006] and [0007] of the present application.

None of the cited references, either alone or in combination, disclose or suggest a method of determining a model for predicting disease risk, where the model itself uses non-genetic data as input but the parameters are optimized using weights which are dependent on the genetic data in their respective data sets. The Examiner has not pointed to any specific reference, or combination of references, that disclose or suggest these features of the claimed method, or that such a method would provide the benefits discussed above. Therefore, it is respectfully submitted that claim 1 is patentably distinguishable from the cited references.

For similar reasons, it is submitted that claims 2 to 15 and 17 to 30 are also patentably distinguishable from the cited references.

The Examiner further rejected claims 1-15 and 17-30 under 35 USC 103(a) as obvious having regard to Dodds in view of Tibshirani and Nelson *et al.* However, the Examiner has not indicated that either Tibshirani or Nelson *et al.* discloses or suggests the feature that is missing in Dodd discussed above. Careful review of Tibshirani and Nelson *et al.* reveals that they indeed do not address the defects of Dodds and Luciano as discussed above. Therefore, the Examiner has again failed to establish a *prima facie* case of obviousness

Thus, withdrawal of the rejections under 35 USC 103(e) is respectfully requested.

No new matter has been added by way of this amendment.

In view of the foregoing, favourable consideration of the application is respectfully requested.

Respectfully submitted,

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September 28, 2007